Inhibitory Control Dysfunction in Drug-induced psychosis

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Abstract:
Inhibitory control dysfunction (ICDD) is a core feature of drug-induced psychosis. The present study focused on the investigation of inhibitory control dysfunction among Nigerian patients diagnosed with drug-induced psychosis (DIP). The assessment tools employed were Stroop colour word test (SCWT), mini-mental state examination (MMSE), and the trail making test (TMT) Parts A and B. 100 participants consisting of patients diagnosed with drug-induced psychosis (n=56, 4 females and 52 males) and a control group of 44 persons (21 females and 23 males) took part in the study. There were statistically significant differences between DIP cases and controls on the assessment tasks measuring inhibitory control. Regression analyses showed that age was a significant predictor of the trail making test (TMT) Part B performance. The results indicate that drug-induced psychosis patients are at higher risk of developing inhibitory control dysfunction than the general population.

Keywords: inhibitory control dysfunction, general cognitive functioning, executive function, drug-induced psychosis, treatment, neural networks, neurochemistry.

INTRODUCTION:

Inhibitory control dysfunction (ICDD) has been found to be a core feature of drug-induced psychosis and a vital component of executive function (EF) [1][2] [3][4]. The concept of executive function first arose from deficits observed in patients with damage to the frontal lobes [5][6]. D.T. Stuss et al [7] in their study of the frontal lobe, identified anticipation, goal selection, preplanning, monitoring, and use of feedback as executive skills and have suggested that the anatomical site of these skills is the prefrontal cortex. Intact executive function is critical to the ability to adapt to an ever-changing world, and deficits in executive function lead to disproportionate impairment in function and activities of daily living [4]. Executive function is predominantly supported by the frontal lobe that regulates lower level processes such as perception, motor responses and thereby generating processes of self-regulation and self-directed behaviour in order to perform a desired task. Its coordinating processes make it possible to break out of undesirable habits, make decisions and evaluate risks, plan for the future, prioritize and sequence our actions in order to cope with changing or novel situations [8] [9] [10]. However, the foregoing definitions fail to provide the essential link between mental processes, structural and functional connectivity and behavioural outcomes. Hence, for the purpose of this research work, we define executive function as the mental processes required to initiate, perpetuate and complete series of goal-motivated behavior necessary for adaptive living. These processes are activated in response to existential, novel or demanding situations and involve the capacity to dynamically adjust behavior according to internal representations or feedback from the environment [11]

In recent times, functional imaging techniques have been the dominant force in cognitive neuroscience because they enable us to determine when and where neural activity in the brain is associated with the ability to perform a particular cognitive task [1][12]. With the advent of functional neuroimaging, it has become clear that executive function relies on distributed complex neural networks that encompass the prefrontal cortex, but also engage the parietal cortex and sub cortical regions. Hence, the executive function system is mediated by numerous networks in the frontal, parietal and occipital cortices, the thalamus and the cerebellum [13]. It is linked through a series of circuits connecting every region of the central nervous system. Research evidence suggests that the various components of executive function (including inhibitory control) may be unique predictors of individual differences in clinically significant behavioural and functional outcomes. [11][13]

A. Diamond [3] views inhibitory control as a core component of executive functions that involves being able to control one's attention, thoughts, emotions and behaviour to override a strong internal predisposition or external stimulus, in order to do what's more appropriate as defined by the current context. Appropriateness of behavior is accordingly defined by prevailing situation.

Similarly, J. Tiego et al [14] posit that inhibitory control involves the suppression of goal-irrelevant stimuli and behavioral responses. Automatic behavioral responses are elicited due to either habit or hope of immediate reward. However, adaptive behavior often require inhibition of the prepotent, previously learned response in order to meet the current goal [15][4]. Inhibitory control comprises cognitive mechanisms which enable individual organisms to neutralize the influence of unwanted thoughts and actions and control same, so as to achieve adaptive behavior [1]. That is, apart from stopping unwanted thoughts and actions, the selection, choice and performance of appropriate goal-motivated actions are determined. The functionality and neurochemistry of these mechanisms are mediated by interactions between the cortical and sub cortical regions of the brain [16]. Inhibitory control dysfunction is therefore a negation of the neural stability of these mechanisms due to either direct assault on the frontal lobes or disruption of the neural connections or neurochemistry of the brain through drug use/abuse [5] [16].

Inhibitory control dysfunction in DIP:

ICDD is present in drug-induced psychosis; and predisposes people to violent behavior [17], high calorie food [18]; and renders them alcohol dependent [19][20], cocaine dependent [21], substance abusers [22], etc. Drug-induced psychosis refers to a medical condition resulting from use/abuse of certain psychoactive substances which interfere with brain connectivity and functionality [2][23]. Concerns over drug-induced psychosis resulting from use/abuse of alcohol, cannabis (Indian hemp/Igboo/Moroko), cocaine and heroin has now assumed global proportions [24][3][25]. A. Fiorentini, et al[26] found that the propensity to develop psychosis is influenced by the severity of use and dependence. This position is also supported by S. Ham, et al [27] who claimed that psychotic symptoms can be elicited in healthy human adults when exposed to drugs. A.I. Jatau et'al [25] noted that world drug report-2019 of the United Nations Office on Drugs and Crime (UNODC) estimated that 271 million (5.5%) of the global population (aged between 15 and 64 years), had used drugs in the previous year [28 UNODC 2019]. According UNODC World Drug Report 2022, about 284 million people aged 15-64 used drugs worldwide in 2020, a 26 per cent increase over the previous decade. Young people were found to be using more drugs, with use levels, as the time covered by the report, in many countries higher than with the previous generation. It reported that in Africa and Latin America, people under 35 represent the majority of people being treated for drug use disorders [29]. Furthermore, L.E. Ethridge et al [30] studied schizophrenia and bipolar/psychotic cases (n=523), their first-degree biological relatives (n=656), and healthy controls (n=223) employing a manual Stop Signal task and found that inhibitory control dysfunction is a trait related to psychotic illness processes. The major drawback of the study is its failure to include alcohol, cocaine, cannabis and heroin cases among its sample. A.D. Arafat et al [31] conducted a study employing neuropsychological investigation of executive function in substance/medication induced psychosis; cases (n-27) and healthy controls (n=27) and found evidence of inhibitory control dysfunction among clinical cases. However, the sample size was comparatively small and test of general intelligence was overlooked. In general, very little research has been carried out on cognitive inhibitory control impairment in drug-induced psychosis. And in particular, there is paucity of such studies in Nigeria.

In the present study we used the stroop colour word test, trail making test parts A and B and mini-mental state examination to test for the presence of inhibitory control dysfunction in patients diagnosed with psychosis resulting from use/abuse of alcohol or cannabis or cocaine or heroin.

We hypothesized that
1. Test scores would reflect inhibitory control dysfunction among DIP patients.
2. There would be significant differences distinguishing DIP cases from control groups on SCWT and TMT
3. MMSE performance of clinical group would be poorer than that of the control group.

Method:

Sample

A total of 100 participants (n=25 females and n=75 males aged between 18 and 68 years were included in the study. This included a sample consisting of fifty-six Drug-induced Psychosis patients selected after consent was obtained at the In-Patient and Out-Patient departments of Federal Neuropsychiatric Hospital, Benin City; Nigeria There was a control group of forty-four volunteers. The control group was drawn largely from religious communities with a demonstrable aversion to smoking, alcohol and drug use [24] .

Instruments:

The following instruments were used in the study:

1. Subtests of the Mini-mental state examination (MMSE) 2.Trail Making Test (TMT) Parts A and B 3. Stroop colour word test (SCWT). See R. Lawani and S.Tomar[2] for details.

The Trail-making Test (TMT) is a standard measure of executive function and inhibitory control ability in particular as well as attentional abilities. It is an easily administered paper and pencil test and is a standard component of the Delis-Kaplan executive function System (DKEFS)[32 Bhatia..]. There are two parts of this test: Part A (numbers) and Part B (numbers and alphabets alternating with each other) [4]. Performance was considered to be impaired if scores exceeded 40 seconds for Part A and 91 seconds for Part B of TMT when the test was administered to English-speaking American subjects [32 Bahtia et al]. Healthy Nigerian subjects were found to perform on the TMT within the range of these normative values.

Procedure:
Cases were individuals diagnosed with drug-induced psychosis resulting from the use/abuse of cannabis, alcohol, cocaine or heroin and were recruited after ethical clearance from the Federal Neuropsychiatric Hospital, Benin City, Nigeria Ethics Committee was received.. All subjects who met inclusion criteria were recruited. Cases and controls were personally administered the mini mental status examination (MMSE), TMT Parts A and B; and SCWT by this researcher between the months of June, 2021 and January, 2022. Time taken to complete all parts of the test and scores were recorded. Demographic and clinical details were also recorded for all participants. See Lawani & Tomar [2] for details of instructions to participants on the mini mental state examination (MMSE), TMT Parts A and B. In the Stroop color word task, participants verbally named (in five seconds), and the color of "color" words printed in different colors: yellow printed in red, blue printed in yellow, green printed in blue, red printed in green.

Ethical Compliance:
Ethical approval was by Research Ethical Committee of Federal Neuropsychiatric Hospital Benin City, Edo State, Nigeria. [NO.PH/A.864/VOL.XIX/84]

Statistical Analysis:The above neuropsychological tests were administered, scoring done according to the standard procedure as prescribed in the manuals. Data were evaluated on required statistical techniques with descriptive details. Statistical analyses were conducted using IBM SPSS Statistics version 20.0 (IBM, Armonk, NY, USA)

RESULTS:
Table 1 Mean (M) and Standard Deviation (SD) for Study Variables with N=56 (Clinical Group) and N= 44 (Control Group)

	Drug-induced psychosis (clinical group)		Control Group	
Variables	*M*	*SD*	*M*	*SD*
Age	32.7857	8.97818	31.90	14.46
Schooling years	13.1339	2.30512	13.43	1.96
ORIENTATION OF PARTICIPANT	8.05	2.37	9.7045	1.06922
Memory	2.1786	2.88007	2.4545	.97538
ATTENTION	3.5893	1.97048	4.4091	1.26341
Recall	2.6607	2.67838	2.7273	.69428
Language	5.5179	2.36636	6.4318	2.60052
Total MMSE	21.1607	4.53983	25.11	4.45
TMT Part A	100.1429	76.92084	54.59	18.82
TMT Part B	193.2321	89.32555	98.95	40.45
Stroop colour word test (SCWT)	2.1964	2.03085	3.09	2.11
Duration of illness	1.6548	5.22824	Not Applicable	Not Applicable

Demographic characteristics:
The mean ages (standard deviations, *SD*) of the cases and controls were 32.78 (*SD*=8.97) and 31.90 (*SD*=14.46) years respectively. There were no significant differences between mean ages of cases and controls (t=1.007, P= .319>0.05). Gender-wise distribution of the sample was 7.7% females, 92.38% males among cases and 47.7% females, 52.3% males among controls. There was significantly more number of males than females among drug-induced psychosis cases. The mean years of education *SD*) were comparable: for cases 13.13 (*SD*=2.30) and controls 13.43 (*SD*=1.96). There were no significant differences between cases and controls on schooling years.

Table 2 Comparison of means for Drug-induced psychosis and Control Group orientation scores

	Test Value = 9.70			
	t	Sig. (2-tailed)	95% Confidence Interval of the Difference	
			Lower	Upper
orientation score of DIP participants	-5.183	.000	-2.2831	-1.0098

Table 3 Comparison of means for Drug-induced psychosis and Control Group attention scores

	Test Value = 4.40			
	t	Sig. (2-tailed)	95% Confidence Interval of the Difference	
			Lower	Upper
attention score of DIP participants	-3.079	.003	-1.3384	-.2830

Table 4 Comparison of means for Drug-induced psychosis and Control Group LANGUAGE scores

	Test Value = 6.43			
	t	Sig. (2-tailed)	95% Confidence Interval of the Difference	
			Lower	Upper
language score of DIP participants	-2.885	.006	-1.5459	-.2784

General Cognitive functioning: case-control comparisons:

Analysis of the research data obtained began with a comparison of the clinical group versus the control group with respect to all measured cognitive functions. Table 1 shows average results of all tests and subtests used in the study. General cognitive functioning assessment data revealed consistent evidence indicating a uniform impairment in inhibitory control of DIP cases compared with controls. Notably, cases performed significantly worse than controls on *orientation* (t= 5.18 p<0.001); *attention* (t= 3.07, p=0.003); *language* (t= 2.88, p=0.006) .Total MMSE scores, Cases 21.16 (SD=4.53) and controls 25.11(SD=4.45) (t=6.51, P<0.001). Cases recorded poorer mean scores than controls on memory and recall subtests of general cognitive functioning. However, the mean differences were not significant.

Table 5 Comparison of means for Drug-induced psychosis and Control Group TMT Part A scores

	Test Value = 54.59			
	t	Sig. (2-tailed)	95% Confidence Interval of the Difference	
			Lower	Upper
TMT A SCORE OF Drug induced psychosis patients	4.432	.000	24.9533	66.1524

Table 6 Comparison of means for Drug-induced psychosis and Control Group TMT Part B scores

	Test Value = 98.95			
	t	Sig. (2-tailed)	95% Confidence Interval of the Difference	
			Lower	Upper
TMTB SCORE OF Drug induced psychosis patients	7.899	.000	70.3606	118.2037

Table 7 Comparison of means for Drug-induced psychosis and Control Group Stroop colour word test scores

	Test Value = 3.09			
	t	Sig. (2-tailed)	95% Confidence Interval of the Difference	
			Lower	Upper
STROOP WORD COLOUR TEST SCORE of Drug induced psychosis patients	-3.293	.002	-1.4374	-.3497

Inhibitory control dysfunction analysis:

There were significant differences between cases and controls on Part A of the TMT. DIP cases (100.14; *SD*=76.92secs) took significantly more time than controls (54.59; *(SD*=18.82secs) (t= 4.43, *p<0.001*) [see Tables 1 and 5] On Part B of the TMT, cases (193.23 (*SD*=89.32.secs) took significantly more time than controls as well (98.95; *SD*=40.45secs) (t =7.89, *p* <0.001) [Tables 1 and 6]. Similarly, the Stroop colour word test performance of cases 2.19 (*SD*=2.03) was significantly worse than controls 3.09 (*SD*=2.11) (t= 3.29, *p = 0.002)* [Tables 1 and 7].

Table 8: Regression analysis showing age as positive predictor of DIP patients TMT Part B performance

Model	t	Sig.	95.0% Confidence Interval for B	
			Lower Bound	*Upper Bound*
(Constant)	1.373	.175	-26.425	141.255
age of Drug induced psychosis patients in years	3.365	.001	1.675	6.611

Table 9: Regression analysis showing MMSE scores as predictor of DIP patients TMT Part B performance

Model	t	Sig.	95.0% Confidence Interval for B	
			Lower Bound	*Upper Bound*
(Constant)	8.539	.000	319.133	514.984
TOTAL MMSE SCORE of Drug induced psychosis patients	-4.685	.000	-15.104	-6.051

***Analyses among patients*:**
Regression analyses were performed to test for effects of different demographic variables on MMSE, TMT, and SCWT; Variables selected for analyses were age, duration of illness and school years. Analysis suggested that higher scores on Part B of the TMT scores were positively predicted by age and general cognitive functioning. (t=3.30, *P=0.002*); (t=4.68, *P*<0.001) [Tables 8 and 9].

DISCUSSION:
The major finding of this study was that drug-induced psychosis cases performed worse than controls on neuropsychological assessment of inhibitory control. To our knowledge, this is about the first report of inhibitory control dysfunction among drug-induced psychosis patients in Nigeria. General cognitive functioning assessment data revealed consistent evidence indicating a uniform impairment in inhibitory control of DIP cases compared with controls, which is a confirmation of previous reports by M. Y. Gotra et al [33]. We found that subjects diagnosed with drug-induced psychosis performances in assessment tasks showed significant inhibitory control dysfunction in agreement with earlier reports by M.T. Fillmore et al [34] and L.E Ethridge et al [30]. The former found evidence of impaired inhibitory control of behavior in chronic cocaine users in a study conducted in 2014, while the latter reported ICDD in a study that focused on behavioural response inhibition among a sample of psychotic disorder patients. DIP cases performed significantly worse than controls on Parts A and B of the TMT assessing inhibitory control component of executive function ability. This aligns with the findings of A.D. Arafat et al [31] who found evidence of ICDD in a study of executive function in substance-Induced psychotic patients in Jordan. Age has been found to adversely affect inhibitory control component of executive function, but the effect was pronounced among drug-induced psychosis cases more than controls. Given that cases are drug-induced psychosis patients, psycho pharmaceutical and psychotherapy approaches in the treatment, rehabilitation and training in cases of ICDD in psychosis should aim to restore homeostatic balance between excitation and inhibition in order to achieve neural stability [35]. It may be necessary to evolve comprehensive training paradigms that involve parents, caregivers, professionals in the field, etc with reference to the stages of human development [36], in view of the pervasive nature of ICDD. The need for inhibitory control training is further underscored by the fact that while psychotic and other psychiatric symptoms generally respond to medication and psychotherapy, cognitive impairments often interfere with full functional recovery, jeopardizing the ability to achieve vocational success and adaptive living [38][39]. The findings of this study are rather disturbing because, many real-life situations require the active inhibition of prepotent actions, as in the case of traffic lights turning red or of criminal actions including financial crimes and fraud involving government and corporate functionaries across Africa, America, Asia, Australia and Europe. [40][41]. And even in clinical settings violence, assault on staff and fellow inmates and destruction of properties that often occur at the facilities may be due to impaired inhibitory control [42][43].

Furthermore, inhibitory control dysfunction has serious implications for personal and societal functioning. Socioeconomic and familial problems are rife among alcohol, cannabis, cocaine and similar psychoactive drug users. Drug-induced psychosis and drug dependence are harmful to family life as a result of neglect, profitless dissipation of family income and inappropriate behaviour. [41][39]. Here, etiology of psychosis is traceable to the influence of alcohol, cannabis, cocaine or heroin without brain lesion or injury or ablation. Hence, inhibitory control dysfunction status among this sample may suggest that neural connectivity and neurochemistry of the brain were disrupted [44][45].Nevertheless, we may not rule out cross-disorder overlap and within-disorder variability [45]. ICDD could predict drug-induced psychosis.

The findings showed that drug-induced psychosis patients are more vulnerable to inhibitory control dysfunction than the general population.

There are limitations worth noting in this research work. The study sample could have been larger with a broader geographical spread in order to improve its validity and generalizeability. Moreover, a lot more assessment tools that could detect inhibitory control dysfunction might have been included. Future research may consider including greater number of subjects and additional inhibitory control assessment tools.

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